Case Report

Kounis syndrome resulting from anaphylaxis to diclofenac

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ABSTRACT

"Kounis syndrome" refers to acute coronary syndromes of varying degree (myocardial ischaemia to infarction) induced by mast cell activation as a result of allergic and anaphylactic reactions. ST-segment elevated myocardial infarction is a rare complication that can occur even in patients with normal coronary arteries due to anaphylactic reactions. We present a case that developed acute myocardial infarction following a diclofenac sodium-induced anaphylaxis. The patient did not have any previous coronary artery disease, but there was a temporal relationship with development of the anaphylactic reaction due to diclofenac sodium and the cardiac event. The patient was managed conservatively and the recovery was uneventful.

Key words: Anaphylaxis, diclofenac sodium, Kounis syndrome, myocardial ischaemia/infarction

INTRODUCTION

"Kounis syndrome" was first described in 1991 by Kounis and Zafras. It is also known as "allergic angina syndrome" or "allergic myocardial infarction".[1] We report a case of Kounis syndrome induced by diclofenac sodium in a patient with previously normal coronary vessel. The aim of presenting this case report is to highlight this rare syndrome, which is caused by one of the most commonly administered drugs in the hospital set-up. Physicians should be aware of such a complication to make a prompt diagnosis and initiate an early treatment.

CASE REPORT

A 64-year-old man was admitted for surgical correction following fracture of both bones of the left leg. During pre-anaesthetic check-up, his blood pressure was recorded as 134/86 mmHg and pulse rate was 70/min. The patient was not a known smoker or alcoholic. There was no history of allergy, bronchial asthma or any previous surgeries. His functional capacity was 7 metabolic equivalents. His airway was graded as Mallampatti class 2. Systemic examination was normal. All investigations, including kidney function, haemogram, urine, random blood sugar, electrocardiogram and chest X-ray, were within normal limits. He was accepted for anaesthesia under ASA physical status class I.

In the ward, the patient complained of severe pain and was given diclofenac sodium 50 mg intramuscular in the gluteal region. Ten minutes thereafter, the patient developed chest pain and pruritus over the lip along with redness and wheal over the site of injection. His blood pressure was found to be 70/54 mm of Hg with a heart rate of 104 beats per minute. Electrocardiography (ECG) showed ST-segment elevation in leads II, III and avF. An ST-segment elevation myocardial infarction (STEMI) of inferior wall was diagnosed and, following primary management, the patient was immediately shifted to the intensive care unit and cardiology consultation was sought. Detailed physical examination of the patient revealed diffuse erythema and rash primarily over the trunk, allergic etiology of the cardiac event was considered in view of the clinical history and temporal relationship with intramuscular diclofenac sodium injection.

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Treatment was started with 0.1 mg adrenaline (1 in 10,000) and 10 mg chlorpheniramine maleate IV, along with 125 mg of methyl prednisolone. Intravenous administration of fluid was continued. Emergent coronary angiography revealed normal coronary vessels. The troponin T level was found to be elevated, but levels of creatine kinase (56 units/L) and creatine kinase-MB (3 units/L) fractions remained normal.

The patient's blood pressure by this time was 104/68 mmHg. The rashes disappeared completely over the next 2–3 h and the electrocardiographic findings returned to normal. Serum tryptase however was found to be elevated, which was done before shifting the patient to the cath lab and also 2 h after the coronary event. The patient was discharged to home after conservative management for the fracture and asked to come for surgery at a later date.

DISCUSSION

Kounis syndrome is defined as "the coincidental occurrence of chest pain and allergic reactions accompanied by clinical and laboratory findings of classic angina pectoris caused by inflammatory mediators released during the allergic insult".[2] The underlying pathophysiology in Kounis syndrome is coronary artery vasospasm due to release of vasoactive mediators secondary to mast cell degranulation.[3] During mast cell degranulation, several vasoactive compounds (histamine, leukotrienes and serotonin) and collagen-degrading compounds (neutral proteases) are released, causing a powerful vasoconstriction in the coronary arteries.[2] These mediators may act locally or systematically. Among the mediators released, the important ones are histamine, serotonin and leukotrienes.

Histamine has also been implicated for activation of platelets and for triggering thrombosis.[4] The mast cells in the heart tissue participate in anaphylaxis and trigger tachycardia, alter ventricular contractility and block atrioventricular conduction, leading to heart blocks of varying degrees. Rennin is also released during episodes of anaphylaxis and can lead to heart dysfunction.[5] Continuous or delayed allergen absorption may aggravate anaphylaxis further, and a late-phase reaction represents a potential risk in all anaphylactic reactions. Treatment with adrenaline, antihistamines and corticosteroids should be initiated in addition to coronary intervention. Cardiac anaphylaxis[6] is the term proposed for the same, and it refers to the functional and metabolic changes occurring in the heart following an allergic reaction, caused by the release of histamine and metabolites of the arachidonic acid cascade.

Kounis syndrome has been classified into two main types.[4] Type I patients have normal coronary arteries and symptoms develop as a result of endothelial dysfunction without increase in cardiac enzymes and troponin. Type II patients include those with culprit but quiescent coronary disease, and they have associated rise in cardiac enzymes and troponin. Our patient suffered from type I Kounis syndrome. A new type III variant includes patients with coronary thrombosis where the aspirated thrombus shows presence of eosinophils and mast cells.

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly implicated class of medications causing anaphylaxis,[7] and aspirin-induced myocardial infarction has been reported before.[8] Because of the wide usage of NSAIDs, knowledge of this syndrome holds a special importance for the anaesthesiologist. As observed in our case, the patient reported symptoms related to acute myocardial ischaemia after administration of intramuscular diclofenac sodium for pain relief; hence, the diagnosis of Kounis syndrome was made.

The multifactorial aetiology of Kounis Syndrome usually mandates a very detailed and careful clinical evaluation. We asked for any history of atopy, bronchial asthma and nasal polyp from the patient. Even the previous medical records were checked for any possible drug hypersensitivity and intolerance that patient was not aware of. The patient also denied any previous episode of coronary artery disease.

Role of mast cell membrane stabilisation drugs has also been put forward as a therapeutic strategy in patients having allergy/anaphylactic reaction and in those experiencing allergic infarction.[9-10]

CONCLUSION

Myocardial Infarction with elevated ST-Segment is a rare complication of anaphylactic reactions, but can occur even in patients with angiographically normal coronary arteries, and similar cases have been reported before. We recommend that ECG be done in all patients developing hypersensitivity reactions. In case a previously normal patient develops acute

coronary spasm, all possible causes of allergy should be looked for.

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